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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Campbell et al
Serial No: 09/117,823
For: Famciclovir Monohydrate
Art Unit No: 1611
Examiner: Mark L Berch

DECLARATION OF MICHAEL JOHN RAW

I, Michael John Raw, hereby declare:

1. That I am Michael John Raw of SmithKline Beecham p.l.c., New Frontiers Science Park, Harlow, Essex, CM19 5AW, United Kingdom. I was awarded the degree of Bachelor of Science (Applied Chemistry) in 1984 from Hatfield Polytechnic (now the University of Hertfordshire). Since 1982 I have been employed by Beecham Group p.l.c. and SmithKline Beecham p.l.c. in various capacities relating to analytical chemistry. At the present time, I am an investigator in the Department of Analytical Sciences.

2. I have read and understood the present application US Serial No. 09/117,823 which relates to famciclovir monohydrate. I have also read and understood Harnden *et al*, *J. Med. Chem.*, 1989, 32(8), 1738.

3. I am familiar with the technique of elemental analysis.

4. Elemental analysis involves the oxidation of a known mass of the organic compound to be investigated to form a mixture of carbon dioxide, water and nitrogen oxides. The amount of carbon dioxide produced is measured and this value is mathematically converted to a percentage carbon figure by taking into account the weight of the sample and comparison of the detector response to standards. The carbon dioxide is removed from the system, the amount of water produced is then determined and this measurement is converted to a percentage hydrogen value by a similar process. The water is then removed and the percentage nitrogen in the sample is similarly calculated. The accuracy of this technique is +/-0.4%.

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5. The expected elemental analysis for famciclovir monohydrate ($C_{14}H_{21}N_5O_5$) is:

% Carbon 49.55
% Hydrogen 6.24
% Nitrogen 20.64

6. The expected elemental analysis for famciclovir anhydrate ($C_{14}H_{19}N_5O_4$) is:

% Carbon 52.33
% Hydrogen 5.96
% Nitrogen 21.80

7. Harnden *et al.*, in the Experimental Section for production of Compound 14 (last paragraph on page 1741 and paragraph boarding p 1742) provides for percentages of carbon, hydrogen and nitrogen obtained from the elemental analysis of Compound 14 (p 1742, line 8). The analysis demonstrates that Compound 14 produced and tested in accordance therein was (according to p 1741, paragraph 3, line 10) within +/- 0.4% of the calculated values for famciclovir anhydrate (*i.e.* $C_{14}H_{19}N_5O_4$). Harnden *et al.* incorrectly states in the last line of the paragraph boarding p 1742 that Compound 14 has the formula $C_{14}H_{18}N_5O_4$. This is obviously a clerical error as Compound 14, according to Scheme 1 on p 1739, clearly has the formula $C_{14}H_{19}N_5O_4$. Paragraphs 5 and 6 (above) show that the elemental analysis of famciclovir monohydrate would give a very different percentage of carbon, hydrogen and nitrogen to that of famciclovir anhydrate. The skilled person would therefore recognise that this clearly indicates that Compound 14 is famciclovir anhydrate, and not famciclovir monohydrate as the measured elemental analysis of famciclovir monohydrate would not lie within +/-0.4% of that calculated for famciclovir anhydrate.

8. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardise the validity of this application or any patent issuing thereon.

Date: 11 December 2000

M. J. Rao.

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

FAMCICLOVIR HYDRATE FORM

the specification of which (check one)

☐ is attached hereto.

☒ was filed on 04 February 1997 as Serial No. PCT/EP97/00523
and was amended on (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)

Number	Country	Filing Date	Priority Claimed
9602403.9	Great Britain	07 February 1996	Yes
9618494.0	Great Britain	05 September 1996	Yes

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below.

<u>Application Number</u>	<u>Filing Date</u>
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I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s) or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

Serial No.	Filing Date	Status
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I hereby appoint the practitioners associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and direct that all correspondence be addressed to that Customer Number:

Customer Number 20462.

Address all correspondence and telephone calls to Dara Dinner, SmithKline Beecham Corporation, Corporate Intellectual Property-U.S., UW2220, P.O. Box 1539, King of Prussia, Pennsylvania 19406-0939, whose telephone number is 610-270-5017.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Inventor's Signature: Kenneth Churchill Campbell Date: 25 AUGUST 1988

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